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Unusual formation of cyclic-orthoesters by Pd(II)-mediated cyclization–carbonylation of propargylic acetates

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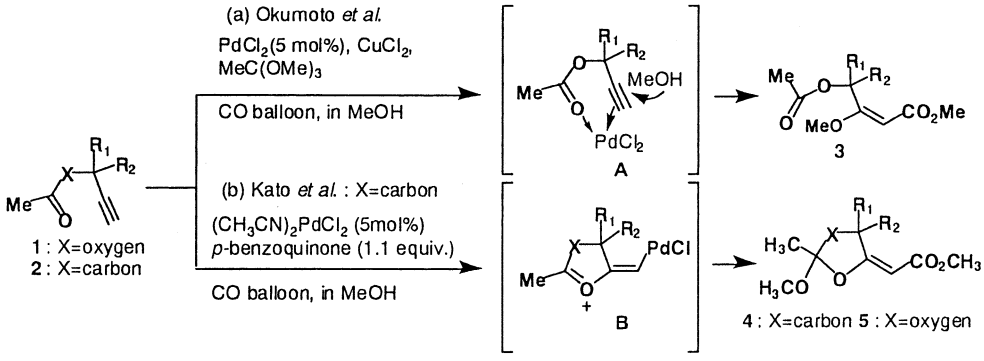
Abstract—The oxidative cyclization–methoxycarbonylation of propargylic acetates **1** in the presence of $(CH_3CN)_2PdCl_2$/*p*-benzoquinone in methanol under carbon monoxide atmosphere (balloon) afforded (*E*)-cyclic-orthoesters **5** in moderate yields. © 2002 Elsevier Science Ltd. All rights reserved.

The reaction of carbon monoxide with alkynes mediated by palladium is a useful method for the synthesis of acetylene carboxylate,[1] γ-lactones,[2] benzofurans[3] and β-alkoxy acrylates.[4] Propargylic esters undergo a number of palladium-catalyzed, synthetically useful transformations,[5] such as preparation of enynes[6] and allenes,[7] nucleophilic substitution,[8] oxidative rearrangement,[9] and carbonylation reactions.[10] Recently, Okumoto et al.[10a] reported the palladium-mediated carbonylation of propargylic acetates **1** afforded γ-acetoxy-β-methoxyacrylates **3** via the direct attack of MeOH to the triple bond of the coordinated intermediate **A** (Scheme 1(a)). On the other hand, Utimoto et al.[11] reported the regioselective hydration of alkynes controlled by neighboring group participation of the carbonyl group. In addition, we have reported oxidative cyclization–carbonylation of 4-yn-1-ones **2** using a Pd(II)/*p*-benzoquinone catalytic system afforded cyclic-ketals **4** via the cyclic intermediate **B** (Scheme 1(b), X = carbon).[12] We considered that similar neighboring group participation of the carbonyl group in propargylic acetates is important for the carbonylation of propargylic acetate **1**. Now we wish to report here the unusual formation of cyclic-orthoesters **5** by the cyclization–carbonylation of propargylic acetates mediated by palladium (II) (Scheme 1(b), X = oxygen).

The oxidative cyclization–carbonylation of propargylic acetate **1a–d**[13] in the presence of $(CH_3CN)_2PdCl_2$/*p*-benzoquinone in methanol at 0°C–room temperature under carbon monoxide atmosphere (balloon) afforded (*E*)-cyclic-orthoesters **5a–d** in moderate yields (Table 1, entries 1–4).[14] In our case, methoxyacrylates **3** were not obtained.[15] The reaction of TBDMS ether **1e** did not



Scheme 1.

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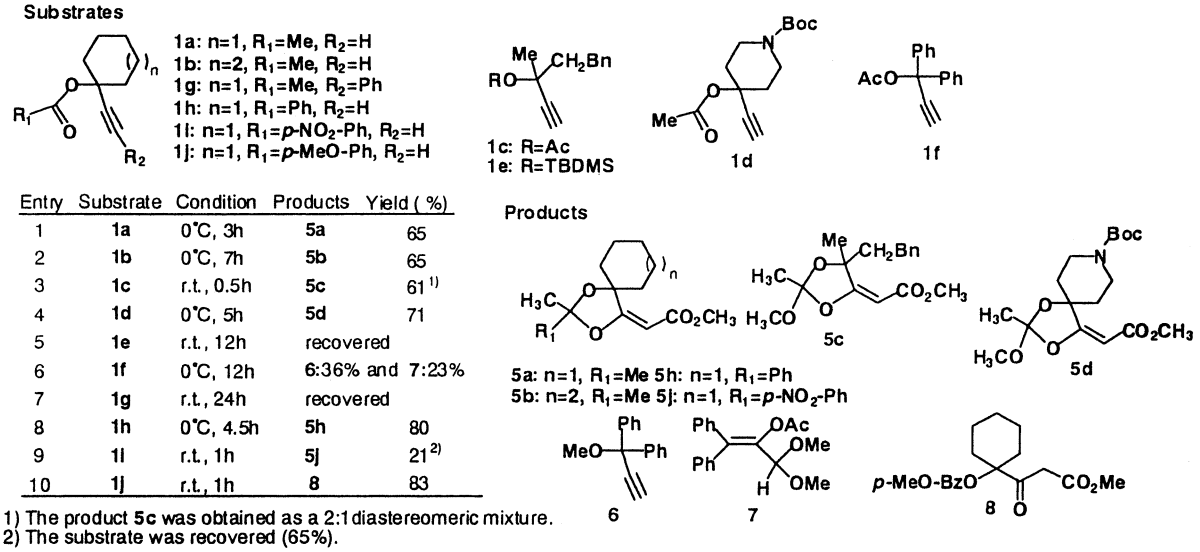
Table 1. Cyclization–carbonylation of propargylic acetate **1**



Entry	Substrate	Condition	Products	Yield (%)
1	1a	0°C, 3h	5a	65
2	1b	0°C, 7h	5b	65
3	1c	r.t., 0.5h	5c	61[1)]
4	1d	0°C, 5h	5d	71
5	1e	r.t., 12h	recovered	
6	1f	0°C, 12h	6:36% and	7:23%
7	1g	r.t., 24h	recovered	
8	1h	0°C, 4.5h	5h	80
9	1i	r.t., 1h	5j	21[2)]
10	1j	r.t., 1h	8	83

1) The product **5c** was obtained as a 2:1 diastereomeric mixture.
2) The substrate was recovered (65%).

proceed under similar reaction conditions, which suggested that the presence of neighboring group participation of the carbonyl group is indispensable for initiating the reaction (entry 5). The substrate **1f**, bearing two phenyl groups in propargylic position, afforded different products **6** (36%) and **7** (23%) from those of entries 1–4 (entry 6). These products **6** and **7** should be produced by S_N1-type substitution of the acetoxy group with MeOH and by oxidative rearrangement of propargylic acetate,[9] respectively. The reaction of internal acetylene **1g** did not proceed and the substrate was recovered (entry 7). Next, we examined the reaction of three kinds of acyl substrates **1h**~**j**. When the benzoate **1h** was subjected to similar reaction conditions, the yield of the product **5h** was improved in comparison with acetate **5a** (entry 8). However, in the case of *p*-nitrobenzoate **1i** having an electron-withdrawing group, the reaction scarcely proceeded and **5i** was obtained in 21% yield together with recovery of the substrate (65%) (entry 9). The use of *p*-methoxybenzoate **1j** bearing an electron-donating group gave β-ketoester **8** in 83% yield. In addition, a similar reaction of **1c** in the absence of CO and *p*-benzoquinone was examined as shown in Scheme 2. Treatment of propargylic acetate **1c** with 5 mol% of $(CH_3CN)_2PdCl_2$ in methanol at room temperature under air atmosphere provided hydroxy ketone **9** and its dimethyl ketal **10** in 49 and 39% yield, respectively. On the other hand, the reaction of TBDMS ether **1e** did not proceed under the same reaction conditions, and the substrate **1e** was recovered quantitatively. These results suggested that the neighboring group participation of the carbonyl group in acetates plays an important role in the Pd(II)-mediated reaction of propargylic acetates.

Selected data of NMR spectra measured in CD_3COCD_3 of **5a** are shown in Fig. 1. The quaternary carbon of orthoester appeared in 124 ppm and its HMBC correlations with proton of the methyl group (1.6 ppm) and with proton of the methoxy group (3.24 ppm) were clearly observed. These results indicated the presence of an orthoester structure. The stereochemistry of **5a** was confirmed by NOE experiment after conversion into allyl alcohol **11** by reduction with DIBAL-H as shown in Fig. 2. The plausible mechanism of the present reactions would be proposed as shown in Scheme 3. Propargylic acetate **1** reacts with Pd(II) to generate vinyl palladium intermediate **C**, which was subjected to

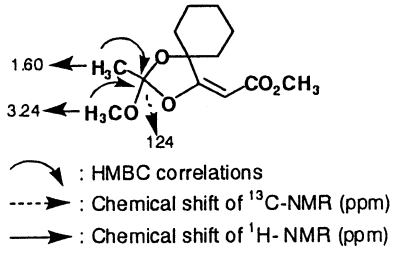


Figure 1. Selected data of ^1H and ^{13}C NMR and HMBC spectra of **5a**.

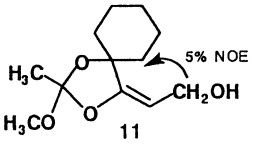
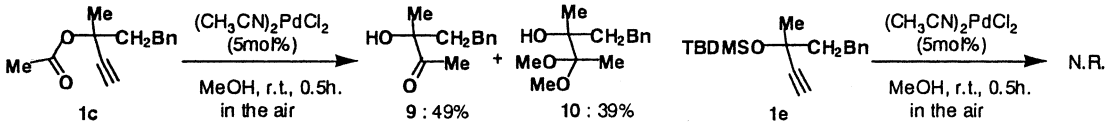
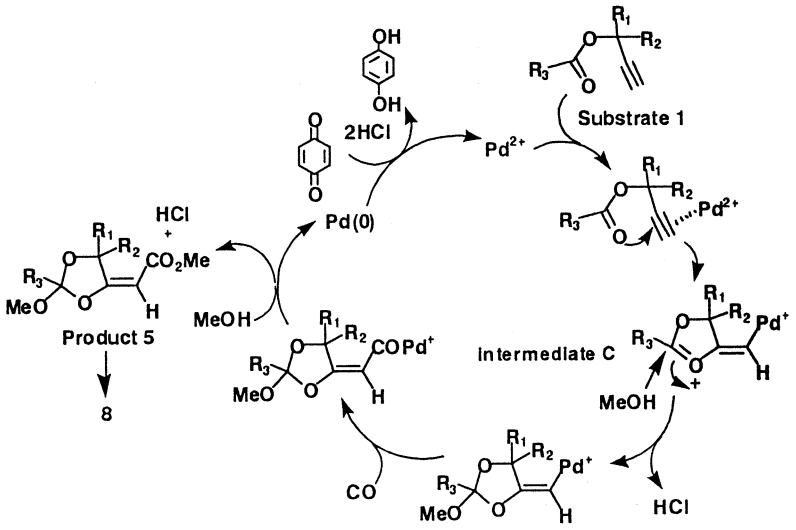


Figure 2. NOE correlation of **11**.



Scheme 2.



Scheme 3.

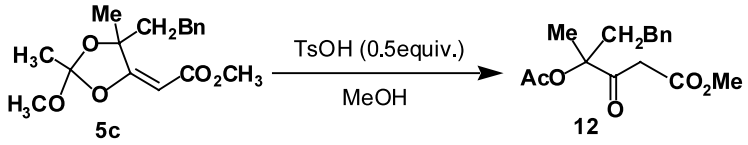


Figure 3.

the nucleophilic attack of MeOH on the carbon atom of the carbonyl group followed by CO insertion to provide the orthoester products **5**. In the case of benzoate **1h** and *p*-methoxybenzoate **1j**, the cationic intermediate **C** (R_3=Ph and *p*-MeO-Ph) should be stabilized by an electron-donating group, and nucleophilicity of the carbonyl oxygen should be increased. Therefore, the yield of the products could be improved. While the electron-withdrawing effect of the nitro group caused decreased nucleophilicity of the carbonyl oxygen in **1i**, the reaction scarcely proceeded. In the case of *p*-methoxybenzoate **1j**, the orthoester bond of **5** (R_3=*p*-MeO-Ph) should be easily cleaved, to afford β-ketoester **8** in good yield.[16]

In summary, we have presented a new type of cyclization–carbonylation of propargylic acetates **1** using a Pd(II)/*p*-benzoquinone catalytic system under mild conditions. The neighboring group participation of the carbonyl group in acetates plays an important role in the Pd(II)-mediated reaction of propargylic acetates.

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13. Compounds **1a**, **1c** and **1d** are the same substrates as those of reported by Okumoto et al. (Scheme 1(a), Ref. 10a).
14. At first, some kinds of palladium catalysts were examined in cyclization–carbonylation of **1a**. Among them, bis(acetonitrile)dichloropalladium(II) gave good results. General procedure: A 30 mL two-necked round-bottomed flask, containing a magnetic stirring bar, $(CH_3CN)_2PdCl_2$ (0.01 mmol), *p*-benzoquinone (0.22 mmol) and MeOH (4 mL) was fitted with a rubber septum and three-way stopcock connected to a balloon filled with carbon monoxide. The apparatus was purged with carbon monoxide by pumping–filling via the three-way stopcock. A solution of the substrate **1** (0.2 mmol) in MeOH (2 mL) was added dropwise to the stirred mixture via a syringe at 0°C. After being stirred for the period of time, the mixture was diluted with CH_2Cl_2 (30 mL), washed with 5% NaOH aq. (40 mL), and dried over $MgSO_4$. The crude product was purified by column chromatography on silica-gel. The fraction eluted with hexane/ethyl acetate (50/1–30/1) afforded **5** as a colorless oil. Satisfactory analytical data were obtained for all new compounds. Compound **5a**: ^{1}H NMR (400 MHz, CD_3COCD_3): δ 1.33–1.41 (1H, m), 1.60 (3H, s), 1.56–1.70 (6H, m), 1.75–1.81 (1H, m), 2.48–2.57 (1H, m), 2.69–2.71 (1H, m), 3.24 (3H, s, orthoester), 3.61 (3H, s, ester), 5.27 (1H, s); ^{13}C NMR (400 MHz, CD_3COCD_3): δ 22.5, 22.7, 25.2, 25.2, 32.1, 33.2, 49.7 (O<u>Me</u> of orthoester), 51.1 (CO_2<u>Me</u>), 87.4 (quaternary, O-<u>C</u>), 89.2 (OC=<u>C</u>H), 124.1 (quaternary, orthoester), 167.0 (ester), 174.6 (O<u>C</u>=CH). Anal. found: C, 61.22; H, 8.12. Calcd. for $C_{13}H_{20}O_5$: C, 60.92; H, 7.87%.
15. We also examined the carbonylation reaction of **1c** by using a $PdCl_2/CuCl_2$ catalytic system, and **5c** was obtained in 70% yield.
16. The β-keto ester **12** was obtained in 83% yield by acid treatment of orthoester product **5c** (Fig. 3).